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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/934,083	08/22/2001	Yixin Wang	P 280651 A0000364	7368
909	7590	05/18/2004	EXAMINER	
PILLSBURY WINTHROP, LLP P.O. BOX 10500 MCLEAN, VA 22102			LY, CHEYNE D	
			ART UNIT	PAPER NUMBER
			1631	
DATE MAILED: 05/18/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

<b>Office Action Summary</b>	<b>Application No.</b> 09/934,083	<b>Applicant(s)</b> WANG ET AL.	
	<b>Examiner</b> Cheyne D Ly	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 02 February 2004.
- 2a) ☐ This action is **FINAL**.      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 12-27 is/are pending in the application.
- 4a) Of the above claim(s) 19-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12-18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 12-27 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Applicants' arguments filed February 02, 2004 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
2. The new drawing corresponding to Figure 5, filed February 02, 2004, has been accepted.
3. The addition of new claims 18-27 has been acknowledged.
4. Newly submitted claims 19-27 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:
5. Specific to claims 19-27, the new claims are distinct from the elected subjected matter due to the requirement of critical limitations and steps, which are distinct from the elected subject matter of claims 12-17. For example, claim 19 is directed to a method for predicting alternative splicing transcripts using a number of different probes, which requires a step for selecting probes based on a defined threshold. The limitations cited above are not required in the elected invention corresponding to claims 12-17. The completely distinct critical limitations and steps of invention support the undue search burden if they were examined together.
6. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 19-27 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

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7. Claims 12-18 are examined on the merits.

8. NON-FINAL OFFICE ACTION.

### **OBJECTIONS**

9. The amendment filed February 02, 2004 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The amendment introduces the "Serum,...to ensure a proper growth environment" [0033] to replace the phrase "The treatment..be emulated" in the instant specification. It is noted that disclosure of "The treatment..be emulated" is for treatment emulation practice which is different from the proposed amendment of "to ensure a proper growth environment." Further, the support for the disclosure of "Serum,...to ensure a proper growth environment" has not been found anywhere else in the instant specification. Applicant is required to cancel the new matter in the reply to this Office Action.

### **CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH**

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 12-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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12. This rejection is maintained with respect to claim 16, as recited in the previous office action mailed October 02, 2003. The instant rejection has been extended to claims 12-15 and 17, and 18.

#### **RESPONSE TO ARGUMENT**

13. Applicant's argument by pointed to support directed to the limitations of noise and "one cut-off threshold" has been fully considered and found to be persuasive. However, claim 16 remains vague and indefinite due to the limitation of "uninformative probes". The pointed to support discloses "uninformative probes" may be filter out by several cut-off thresholds does not resolve whether an "uninformative probe" is determined by lack of signal or false signal due to non-specific hybridization.

14. Specific to claim 16, lines 5-6, the phrase "uninformative probes" causes the claim to be vague and indefinite because it is unclear what criteria are being used to consider that a probe is "uninformative" (lack of signal or false signal due to non-specific hybridization).

Clarification of the metes and bounds of the instant claim is required.

#### **NEW REJECTIONS**

15. Specific to claim 12, the preamble recites a "method for...using DNA chip expression data"; however, the actual steps of said claim do not recite either a DNA chip or expression data which causes claim 12 to be vague and indefinite. Claim 12 is unclear as to whether the preamble or the method steps control the metes and bounds of the instant claimed invention.

Clarification of the metes and bounds is required. Claims 13-18 are rejected for being dependent from claim 12.

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16. Claim 18 recites the limitation "tasks" in line 2. There is insufficient antecedent basis for this limitation in the claim.

**CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH**

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 14 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. NEW MATTER REJECTION.

19. Specific to claim 14, lines 5-7, the removal of lines 5-7 by claim amendment adds new matter to said claim. The instant specification does not have written description basis as originally filed for amended claim 14 due to the removal of lines 5-7. For example, the broadened claim 14 no longer requires the phenol chloroform extraction and ethanol precipitation step which is a required step for the claimed invention as disclosed by the instant specification (page 9, [0038]). Further, Figure 3 discloses the requirement of the step of "purify and quantify cDNA" which is no longer required by claim 14. The limited disclosure of the instant specification as originally filed does not provide written description support to the amended claim 14.

20. Specific to claim 18, line 2, the recitation “a computer to perform one or more tasks of the method of claim 12” is considered to be new matter because the written description basis as filed for a method for performing one step or only two steps of claim 12 has not been found in the instant specification. It is noted that the instant specification provides support of a system and method comprising performing a plurality of steps (greater than two) for predicting alternative splicing transcripts (Figures 2-6). However, support for a computer to perform one or more tasks (only two) of the method of claim 12 has not been found in the instant specification as originally filed.

#### **CLAIM REJECTIONS - 35 USC § 103**

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

22. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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23. Claims 12-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Emmert-Buck et al. (2000) taken with Schena et al. (1996)

24. Emmert-Buck et al. discloses the use of molecular profiling to produce insights and predictions of function of sequences (page 1109-1110, Molecular Profiling §). The method of Emmert-Buck et al. uses differential gene expression (microarray) for generating new insights for predicting novel splice variance of PB39 mRNA transcript (page 1112, column 1, lines 36-58), as instant claim 12, lines 1-2 and 6-7.

25. Emmert-Buck et al. discloses a second splice variant prediction, which is the protein product of the alternative splice form of said transcript (page 1112, column 1, last line, to column 2, line 2), as in instant claim 13.

26. However, Emmert-Buck et al. does not disclose the limitations to claim 12, lines 3-5, and claims 14-18.

27. Emmert-Buck et al. cites Schena et al. (Citation Number 8) as an author of technologies capable of global gene expression measurements (page 1109, column 2, lines 11-13).

28. Schena et al. discloses a well-known in the art technique for test sample preparation wherein mRNA is extracted from tissues, purified and quantified; and hybridization and scanning are performed for data processing (Schena et al., page 10614, columns 1-2), as in claim 12, lines 3-5, and claim 14.

29. Schena et al. discloses hybridization signals were observed to be greater than 95% (threshold) of the human cDNA array elements, but not for any of the negative controls (Schena et al., page 10615, column 2, lines 6-8 and Figure 1). Each of the tissues samples was normalized to the control (filter) to generate an expression profile for each of the 1046



clones present on the array (Schena et al., page 10617, column 2, lines 6-10). Database searches revealed perfect matches (threshold) for five of the six sequences (Schena et al., page 10617, column 1, lines 20-23). Table 1 contains data as directed to the normalized difference of the two ratios wherein said ratios are greater than half the average ratio. The accession number reflects the highest score for the proximal and distal sequence traces (prioritize) (Schena et al., page 10616, Figure 2 and Table 1), as in instant claims 15 and 17.

30. Table 1 contains data as directed to the normalized difference of the two ratios wherein said ratios are greater than half the average ratio (Schena et al., page 10616, Figure 2 and Table 1). Figure 3 illustrates the tissue specific gene expression values for 15 genes across said tissues. Tissue samples were normalized to the control to generate an expression profile for each of the 1046 clones. Detectable (threshold) expression was observed for all 15 genes in the four specific tissues types examined (across) and the relative expression is determined among the tissues (page 10617, column 2, lines 6-20). The method of Schena et al. comprises determining the final fluorescence ratios by taking the average of the ratios (relative signal strength) of two independent hybridizations (page 10614, column 2, Hybridization and Scanning), as in instant claim 16.

31. The arrays were scanned using a fluorescence laser scanning device (page 10614, column 2, Hybridization and Scanning) and pseudocolor representations of fluorescent images (preprocessing hybridization data of claim 12 (at least one task of claim 12)) were made with National Institutes of Health IMAGE software (computer readable medium with instructions) (Schena et al., page 10615, column 1, Computer Graphics and Informatics §), as in instant claim 18.

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32. Emmert-Buck et al. disclose improvements in biomedical research techniques such as molecular profiling with the potential to increase dramatically our understanding of how cellular mechanisms response to the environment (page 1109, column 2, lines 2-16).

Further, Emmert-Buck et al. cites Schena et al. (Citation Number 8) as an author of technologies capable of global gene expression measurements (page 1109, column 2, lines 11-13) wherein said data is used produce insights and predictions as directed to diseases (page 1109, column 2, Molecular Profiling §). Therefore, the improvement of Emmert-Buck et al. is directly applicable to the method of analyzing cDNA expression data generated from a microarray as taught by Schena et al.

33. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the improvements disclosed by Emmert-Buck et al. and practice the method of predicting alternate splicing transcripts by analyzing cDNA expression data generated by the method of Schena et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to practice the method of predicting alternate splicing transcripts by analyzing cDNA expression data as taught by Emmert-Buck et al. and Schena et al.

### **CONCLUSION**

34. NO CLAIM IS ALLOWED.

35. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61

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(November 16, 1993), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

36. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

37. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

38. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

C. Dune Ly  
5/12/04

*Ardin H. Marschel* 5/14/04  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER